## REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated October 24, 2003. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 1-8 are under consideration in this application. Claim 1 is being amended, as set forth above and in the attached marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim Applicants' invention. New claims 5-8 are being added to recite other embodiments described in the specification.

Additional Amendments

The claims are being amended to correct formal errors and/or to better disclose or describe the features of the present invention as claimed. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

Formality Rejections

The recitation of "said islands are spaced from each other with intervals filled with a heat insulating material" was rejected as constituting new matter. The same recitation was also rejected under 35 U.S.C. §112, first paragraph. As indicated, the recitation has been amended as required by the Examiner. Accordingly, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

Double Patenting Rejection

Non-statutory, obviousness-type double patenting rejection was maintained against claims 1-4 as being unpatentable over claim 1 of the patent issued into U.S Pat. 6,428,749 due to the recitation of "filled with a heat insulating material" is not supported by the specification.

Applicants contend that claim 1 of the application now recites a distinctive limitation of "said islands are spaced from each other with intervals filled with air" that is different from the limitation "a membranous substrate whose heat conductivity is 10 w/mk (watt/(meter • kelvin)) or

less" of claim 1 of the '749 patent. Accordingly, the withdrawal of the outstanding double patenting rejection is in order, and is therefore respectfully solicited.

Prior Art Rejections

Claim 1 was rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 6,093,370 to Yasuda et al (hereinafter "Yasuda") defined Physics: Principles with Application by Giancoli DC (1991). Claim 4 was rejected by Yasuda as defined Giancoli and Handbook of Chemistry & Physics, and claims 2-3 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Yasuda as defined by Giancoli in view of U.S. Pat. No. 6,051,380 Sosnowski et al. (hereinafter "Sosnowski"). These rejections have been carefully considered, but are most respectfully traversed.

The biochemical reaction detection apparatus (e.g. Fig. 2B; page 26, 2nd-3rd paragraphs) of the invention, as now recited in claim 1, comprises: a first membrane; a plurality of islands provided on one side of said first membrane; and probe cells for immobilizing probes for detecting biochemical reactions, each of said probe cells being provided on a side opposite to said one side of said first membrane corresponding to one of the islands though a cross section of the first membrane. The islands are spaced from each other with intervals filled with air (e.g., page 6, line 15), and each of the islands includes a temperature controller for heating and temperature-controlling a corresponding one of said probe cells independently (e.g., page 6, line 17).

The invention provides a plurality of islands on one side of a first membrane, and the islands are spaced from each other with intervals filled with air. Each island corresponds to a probe cell on the other side of the first membrane and has a temperature controller therein. The amount of heat transmission form an object A to an object B through a heat conductive body sandwiched between the objects A and B becomes larger, as the temperature difference between the objects A and B becomes bigger, or as the heat transmitting distance L (which is the length of the heat conductive body put between the objects A and B) becomes shorter, or as the cross section S of the heat conductive body becomes larger. Since the first membrane is 500 μm thick or thinner (preferably 5-20 μm, p. 5, 2nd paragraph), heat can transmit easily from a corresponding temperature controller in one island *vertically* to the probe cell corresponds to the same island. However, there is negligibly small amount of heat transmits *horizontally* from neighboring islands to the probe cell through the first membrane due to the small cross section of the heat transmitting portion of the first membrane. The heat transmits from neighboring islands to the probe cell through the air is even less due to the air's low heat conductivity. Accordingly, the temperature of the probe cell of each island is independently and accurately controlled.

Hence, it becomes possible to independently control the temperature of each of probe cells to an "*optimal temperature for one specific reaction* (p. 16, lines 9-10)" so as to conduct different biochemical reactions in parallel (p. 16, lines 7-8).

None of the cited prior art references teaches or suggests each of such "islands (1) being provided across a membrane from a corresponding probe cell, (2) including a temperature controller for heating and temperature-controlling said probe cell independently, and (3) being spaced from each other with intervals filled with air. Since there is no substantial heat transmission from one island to the other, the temperature of each probe cell can be accurately and separately controlled.

In contrast, each of the alleged islands in Yasuda (Fig. 11) includes a heating element 225 sandwiched between a planar electrode 226 and a planer electrode 224 (Fig. 12C) is spaced from each other with intervals filled with a temperature control unit 133, rather than "**air**". As such, the substrate 133 can't insulate heat *horizontally* as efficient as the invention.

In particular, since the temperature of a specific target polynucleotide hybridization area 221, i.e., an island, is controlled by a potential applied to a pair corresponding electrodes 226, 224 (col. 12, lines 2-11), the material filled between the sandwich structure of 224, 225, 226 must be heat conductive such that the heat evolved by the heating element 225 can be transmitted upward towards a corresponding polynucleotide hybridization area 221, and downwards towards a corresponding thermistor 231 for detecting the temperature of corresponding polynucleotide hybridization area 221 (col. 11, lines 58-62). Inevitably, the sandwich filling material among islands also transmits heat horizontally among different islands. There is simply no mechanism for blocking the heat transmission between adjacent islands in Yasuda.

In Embodiment II (Fig. 11) of Yasuda, several heating element layers 225 are located within one temperature control unit 133, and several thermistors 231 are located within one thermally conductive insulating substrate 132. Specifically, a heating element layer 225 heats the probe hybridization layer 221 through the temperature control unit 133, and this temperature control unit 133 is also in contact with the other heating element layer 225. When the heating element layer 225 emits heat, the heat is transmitted to the other heating element layer 225 through the temperature control unit 133. Accordingly, temperature of a probe hybridization layer 221 is interfered by that of the adjacent probe hybridization layer 221. Further, the thermistor 231 detects temperature of the probe hybridization layer 221 of interest through the thermally conductive insulating substrate 132. At the same time, it detects temperature of the probe hybridization layer 221 existing in the vicinity. Thus, temperature of each probe hybridization layer 221 cannot be accurately controlled according

to the technique of Yasuda.

Regarding the rejection against claim 4, Applicants respectfully contend that the Examiner improperly combined the Embodiment II (col. 11, lines 43-62) and the Embodiment III (col. 13, lines 35-57) of Yasuda (page 5, last paragraph of the outstanding office action), since there is no teaching of combining the two heating methods or combining a temperature controller and a glass substrate in Yasuda. Embodiment II concerns a heating method with the heating elements 225 therein. On the other hand, the Embodiment III concerns a heating method through YAG laser irradiation without any heating elements 225 (lines 49-64, Column 15). It is well established that a rejection based on combining contradictory principles that teach away from each other is improper.

Accordingly, Applicants contend that the cited conflicting teachings of the prior art references would not motivate their combination such that their combination would embody each and every feature of the present invention as now claimed in claim 1, and from which claims 2-5 depend. The difference is more than sufficient that the present invention as now claimed would not have been rendered obvious given the prior art. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of

the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

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